SmithKline Beecham
Pharmaceuticals

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5630 Fishers Lane
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Docket No. 99N-4166

Reference is made to the Federal Register Notice of 1 October 1999. Four specific questions were posed, of which questions (1), (2), and (4) are addressed in this document.

Question (1): Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility.

We welcome the opportunity to use electronic signatures in lieu of traditional handwritten signatures, as it is clear that electronic filing and submission will become the norm for both industry and FDA. Additionally, we find guidance on the use of electronic systems useful. Nevertheless, we emphasize the critical element involved here is "future." As FDA has acknowledged informally, industry is not yet prepared to be in full compliance with Part 11. At a minimum, systems must be purchased and developed which, according to the October 1, 1999 Federal Register Notice (the "Notice"), was not part of FDA's assumptions in drafting the rule. Further, questions have been raised by others about the utility of the data, for example, whether the broad definition of "electronic record" captures information the agency neither needs nor intended to collect.

Despite the fact that the technologies are not in place to facilitate full compliance with Part 11, the FDA is currently able to effectively perform it's functions in reviewing combinations of paper and electronic records. We agree that compliant electronic systems maintained over extended periods of time will enhance the efficiency with which the agency performs its functions in the future. Still, we emphasize there are currently technological and practical issues involved that may not be resolved for many years.

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*Question (2): The accuracy **of** FDA's estimate **of** the burden **of** the proposed collection of information, including the validity **of** FDA's methodology and assumptions used.*

It is difficult to comment on the OMB estimates because little has been published about the underlying assumptions. The Notice implies the agency's estimates pertain only to the last step, creation of SOPs, validation and certification. The Notice also contains a footnote stating "there are no capital costs or operating and maintenance costs associated with collection of this information." We question both of these assumptions, as the definition of "electronic record" is so broad that it touches on practically every system that is even remotely associated with our manufacturing facilities, and requires tracking of some information that simply has no practical application to the operation of our business. To track this data and ensure full compliance, we are required to purchase and develop systems, and are therefore incurring both capital and maintenance costs as a necessary first step prior to performing the record keeping functions outlined in the Notice.

This effort will require as much of a commitment of time as our effort to document Y2K compliance, possibly more.

We feel that the published estimate grossly underestimates the cost of compliance for the pharmaceutical industry by focusing simply on the one time cost of SOPs, validation and certification. The total view would include but is not necessarily limited to the following areas: SOPs, Part 11 training (train the trainer; department level training); inventory and assessment; corrective action plans; implementation of corrective action plans; capital expenditure, validation, electronic archival; and data migration. The total cost of these initiatives for SmithKline Beecham is estimated to exceed 214 million dollars. The projected costs are 11,940 hrs/ $92,000 in 1999; 192,100 hrs / $2 12,105,000 in 2000; $1 ,OOO,OOO in 2001; 204,040 hrs / $2 14,047,000 for 1999 through 2001.

This rule will also have indirect costs to industry. For example, the cost of assuring compliance on the part of third party vendors, e.g., Contract Research Organizations (CROs) will result in additional significant costs. (Those provided above reflect only SmithKline Beecham's internal cost estimates). Since it is expected that the sponsor assure and be responsible for CRO compliance, additional costs in terms of both time and money will be incurred for: (1) more up front work to assess CRO's compliance status; (2) more complex and protracted contract negotiations; and (3) tracking and subsidizing of CRO system improvements by SmithKline Beecham.

*Question (4): ways to minimize the burden **of** the collection **of** information on respondents, including through the use **of** automated collection techniques, when appropriate, and **otherforms of** information technology.*

The following suggestions are made to minimize the burden of compliance:
1. Refining/clarifying the definition of an electronic record in partnership with industry, to cover only what FDA needs, would go a long way to the overly burdensome costs associated with compliance.
2. The retrospective nature of this regulation places great burden on Industry while providing no added value. FDA has acknowledged this burden and, to date, has exercised its discretion in permitting companies both to prioritize their systems, and to achieve compliance in a step-wise fashion. While we applaud FDA's cooperation to date, industry has no formal assurances FDA will continue to exercise Its discretion in this manner. Therefore, we strongly urge FDA to re-consider the effective date of this rule, removing the retroactivity and revising it to reflect more realistically, the timing necessary for full compliance.

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